



DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S.

Government and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Benjamin Hurley at 240-669-5092; benjamin.hurley@nih.gov. Licensing information may be obtained by communicating with the Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, 5601 Fishers Lane, Rockville, MD 20852; tel. 301-496-2644. A signed Confidential Disclosure Agreement will be required to receive copies of unpublished information related to the invention.

SUPPLEMENTARY INFORMATION: Technology description follows:

Producing Modified Vaccinia Ankara (MVA) Virus with Continuous Cell Lines: Modifications of Mammalian Host Cells for Increasing MVA Vaccine Production Yield

Description of Technology:

Modified vaccinia Ankara (MVA) is a well-known and important platform for vaccine development, and many MVA-based vaccine trials are currently underway to prevent a variety of microbial diseases. While MVA shows promise as a vaccine platform, wide-scale industry use of MVA may be currently held back due to MVA's

severe host-restriction, and the fact that large bulks of culture cells are presently required to produce enough product for mass commercial use. At present, the range of commonly-used culture cells that can support high-titer production of MVA is limited to chick embryo fibroblast (CEF) cells. Unfortunately, the production of CEF cells in bulk involves many slow and inefficient manufacturing steps both upstream and downstream. Therefore, especially in the context of pandemic preparedness, continuous cell lines that allow for efficient, large-scale MVA propagation would be beneficial.

There is a clear need for an expanded range of cell lines that are easily maintained in culture, and that allow for the production of high titers of infectious MVA virus. The present invention provides methods of modifying non-permissive cell lines in a way that allows for production of MVA.

Scientists at NIAID have made a breakthrough discovery by identifying the mammalian Zinc finger antiviral protein (ZAP) as a restriction factor that inhibits MVA growth in mammalian cells. They have demonstrated that ZAP abrogation enhanced replication of the MVA in a range of mammalian cells that are normally non-permissive for MVA replication. In particular, CRISPR/Cas9 inactivation of ZAP was shown to produce stable cell lines capable of supporting MVA replication. Additionally, recombinant host cells engineered to produce vaccinia virus proteins C12L and C16L have been shown to overcome the host range inhibition of the MVA.

This technology is available for licensing for commercial development in accordance with 35 U.S.C. 209 and 37 CFR Part 404, as well as for further development and evaluation under a research collaboration.

Potential Commercial Applications:

- Vaccine Development: Recombinant continuous cell lines useful for efficient, large-scale production of MVA.

- May offer improved vaccine production scaling-response times, enhancing epidemic/pandemic preparedness.

Competitive Advantages:

- Overcomes inefficiencies associated with CEF production of MVA-based vaccines.

Inventors: Bernard Moss, Linda Wyatt, Chen Peng, Gilad Sivan, Shira Glushakow-Smith, all of NIAID.

Publications:

Liu R, Mendez-Rios JD, Peng C, et al. SPI-1 is a missing host-range factor required for replication of the attenuated modified vaccinia Ankara (MVA) vaccine vector in human cells.; *PLoS Pathog.* 2019.

Peng C, Moss B. Repair of a previously uncharacterized second host-range gene contributes to full replication of modified vaccinia virus Ankara (MVA) in human cells. *Proc Natl Acad Sci U S A.* 2020.

Peng, C, Wyatt, L, Glushakow-Smith, SG, Lal-Nag, M, Weisberg, AS, and Moss, B. Zinc-finger antiviral protein (ZAP) is a restriction factor for replication of modified vaccinia virus Ankara (MVA) in human cells. *PLoS Pathog.* 2020, accepted for publication

Intellectual Property: HHS Reference No. E-076-2019; International Application No. PCT/US20/33788

Licensing Contact: To license this technology, please contact Benjamin Hurley at 240-669-5092 or benjamin.hurley@nih.gov, and reference E-076-2019.

Collaborative Research Opportunity: The National Institute of Allergy and Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this invention. For

collaboration opportunities, please contact Benjamin Hurley; 240-669-5092,

benjamin.hurley@nih.gov.

Dated: June 2, 2021.

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Technology Transfer and Intellectual Property Office,

National Institute of Allergy and Infectious Diseases.

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